UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/978,636	11/25/1997	ELAZAR RABBBANI	ENZ-53(DIV-3	4642

28171 7590 09/15/2008

ENZO BIOCHEM, INC.
527 MADISON AVENUE (9TH FLOOR)
NEW YORK, NY 10022

EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
09/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/978,636	RABBBANI ET AL.	
	Examiner	Art Unit	
	AMY BOWMAN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *245,247-255,262,265,268 and 269* is/are pending in the application.

4a) Of the above claim(s) *268 and 269* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *245, 247-255, 262 and 265* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 1997* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/17; 6/17; 6/17; 6/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 6/16/08 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 12/26/07 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 245, 247-255, 262, 265, 268 and 269 are pending in the instant application.

This application contains claims 268 and 269 that are drawn to an invention nonelected with traverse in the reply filed on 10/9/07. The claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/9/07.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/16/08 has been entered.

Applicant's arguments and/or amendments to the claims filed on 6/16/08 have been fully considered and are persuasive with respect to the new matter rejection. The examiner thanks applicant for providing a table and pointing with particularity to support for the claim limitations. However, the instant rejections are pending as explained below.

Response to Applicants Arguments-- 35 USC § 112

Claims 245, 247-255, 262 and 265 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection is repeated for the same reasons of record as set forth in the actions mailed 5/31/05, 6/27/06, 4/4/07, and 12/26/07.

Applicant argues that the majority of insertion events would generate frameshift mutations in the coding sequence and inactivate a target gene. Applicant argues that that fact that a frameshift mutation in a transcript will inactivate gene expression is well known in the art. It is agreed that the insertion of an intron into a coding sequence may inactivate gene expression. However, as set forth by applicant, 1/3 of the time, such an insertion will not inactivate gene expression. Therefore, the instant specification does not adequately describe insertion of any intron into any sequence encoding any polymerase in a manner that the construct would necessarily result in being incapable of being expressed in a prokaryotic cell and capability of producing more that one copy of a sequence, not even necessarily the same sequence, when introduced into a eukaryotic cell.

The specification does not set forth any specific structural feature to describe the genus of constructs that would result in the claimed activity. Although applicant asserts that it is a readily ascertainable property to choose an intron candidate, the specification has not described what feature of the intron would necessarily result in the instantly recited outcome. Due to the breadth of the instant claims, one of skill in the art would not be able to readily envision the instant genus of constructs that would be incapable of expression in a prokaryote but capable of producing a nucleic acid sequence in a eukaryotic cell.

Applicant points to the SV40 intron, as disclosed in the specification, and explains that the SV40 intron contains stop codons in all three reading frames. Applicant sets forth mathematical calculations on the probabilities of a codon being a stop codon and points to Schwartz et al. for teaching an intron inserted into a coding sequence that resulted tin a frameshift mutation. Although there are introns in the art that certainly contain stop codons or would result in a frameshift mutation, the specification does not set forth any specific property that would result in incapability of being expressed in a prokaryote while able to produce copies of a transcript in a eukaryote and it is not evident that insertion of any intron would have these results. The Schwartz et al. reference reports on a specific intron that would result in two in-frame stop codons as well as a reading frame shift.

It is important to note that the instant claims are not limited to the embodiments addressed by applicant above. The specification does not provide support for the use of any intron, in any polymerase or any bacteriophage polymerase, or any conditionally

toxic gene, in any eukaryotic or prokaryotic cell because the specification provides only minimal description of any particular intron, polymerase (including bacteriophage polymerase), or toxic gene, or eukaryotic or prokaryotic cells for whom known structures exist that could be utilized having the claimed function.

Applicant asserts that numerous polymerases were known in the art and could have theoretically been used with the present invention. However, the claims do not recite any specific structural element that would allow one of skill in the art to envision the instant genus of constructs and be able to envision which constructs would result in the instantly recited outcomes.

Applicant points to Mount et al. for teachings regarding knowledge of numerous introns. It is agreed that many introns were known in the art, but one of skill would not have been able to envision which ones would act in the context of the instant claims. Regarding "toxic gene", it is acknowledged that the instant specification discusses some examples of a gene being considered toxic in a prokaryotic cell, however the instant specification does not set forth any structural feature that would allow one of skill to envision which genes are considered toxic versus those that are not within the context of the instant claim breadth.

It is acknowledged that it is well known that prokaryotic cells lack splicing machinery that is present in eukaryotic cells. Therefore, the lack of written description is not based upon the differences between prokaryotic and eukaryotic cells, but rather is based upon insertion of any intron into any sequence encoding any polymerase with this resultant action.

The specification provides for the use of T3, T7 or SP6 polymerases, and also for the use of certain "consensus" splice donor and acceptor sites for inserting introns. Applicants prophetically suggest that intron "insertion at any of these sites in a gene coding region should not affect subsequent removal of the processing element in a compatible cell." (page 84 of the instant specification). However, there is significant unpredictability in such intron removal, since such a process requires a complex interaction between the nucleic acid construct and the already existent cellular machinery.

Applicant argues that the (C/A) AGG sites in the target genes resemble a post-splice site and points to Dibb for support of this concept. Applicant argues that these sites will be converted into splice donor and acceptor sites by the addition of the flanking intron sequence. If the presence of a (C/A) AGG site is what applicant is relying upon for the instant mechanism to occur, this should be an aspect of the instant claims. Claim 262 is the only claim that requires a (C/A) AGG site, but the claim is directed to constructs comprising a nucleic acid sequence encoding any gene product, where the specification does not describe that this mechanism would necessarily occur in any gene with a (C/A) AGG site.

Although applicant asserts that splicing is predictable and argues that Balvay et al. reference, Balvay et al. indicates that the splicing machinery is highly dependent upon recognizing and interacting with such secondary structures in making the splice and therefore demonstrates that there are additional considerations in splicing mechanisms. Balvay et al. indicates that the addition of a secondary structure to an

existing mRNA can cause the cell to splice at a point not normally spliced at, while removal of such a structure can cause splicing to be eliminated (for example see pages 165 bridging to 166). Furthermore, Balvay indicates that the exon plays a significant role in splice site recognition by the cellular splicing machinery. Since one of skill would understand that the nucleotides in the exon remain in the mRNA (or ribozyme) after splicing, applicants claimed nucleic acid constructs, following splicing, would likely therefore contain elements of these exon recognition sites. Such unpredictability indicates that the genus of nucleic acid constructs comprising any intron in any polymerase (or any bacteriophage polymerase), or any toxic gene, and that are active or inactive depending on whether they are found in prokaryotic or eukaryotic cells is very large. Regardless of applicant's specific interpretation of the scenarios of Balvay et al., Balvay et al. demonstrates that applicant has not adequately described the instant breadth in a manner that one of skill would be able to readily envision the instant constructs and would not be able to readily envision the specific genus of constructs that would result in the instant outcomes.

Furthermore, applicant asserts that the methods used to block expression are not related to the ultimate function of the protein and therefore the only knowledge necessary would be the sequence of the protein or polymerase so that an appropriate site could be chosen. However, the instant specification does not describe such a broad genus of nucleic acid constructs that would conditionally control the expression of any polymerase or protein sequence based on the presence of any intron in any eukaryotic or prokaryotic cell. The specification does not disclose a structural

characteristic that would allow one of ordinary skill to recognize which introns introduced into which sequences would result in expression or lack of expression of which polymerases or proteins.

Contrary to applicant's assertions, the specific example given in the specification is not representative of the broad genus of nucleic acid constructs that are instantly being claimed. The structural characteristics recited in the instant claims are extremely broad and the specification does not disclose a structural characteristic that would allow for the skilled artisan to envisage the entire genus claimed of nucleic acid constructs with any intron that would result in any polymerase to be incapable of being expressed in any prokaryotic cells and capable of producing a nucleic acid sequence when introduced into any eukaryotic cell. Therefore, the skilled artisan would not be able to recognize that applicant was in possession of such a broad genus of nucleic acid constructs at the time of filing.

Applicant argues that one of skill is fully capable of recognizing the characteristics that would allow a user to choose a particular intron and that SV40 is an example of a wide variety of introns that would be understood to be of use in the present invention. As explained above, one of skill would not be able to readily envision the instant genus of constructs because the claims do not set forth any structural characteristic that would describe which introns inserted into sequences encoding which polymerase would result in the instant activity, as it is acknowledged in the art that there are additional considerations in splicing, as evidenced by Balvay et al., and that the breadth of the instant construct would not necessarily result in the instant outcomes.

Therefore, the teachings of the instant specification coupled with the breadth of the instant claims, is not considered to describe a representative sample of the genus of such constructs that would function as instantly recited.

Claims 245, 247-255, 262 and 265 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. This rejection is repeated for the same reasons of record as set forth in the actions mailed 5/31/05, 6/27/06, 4/4/07, and 12/26/07.

Applicant asserts that Example 19 provides a more than sufficient description regarding strategies used in choosing intron sequences to be used, insertion sites in the T7 polymerase and vectors, as well as construction steps. It is noted that the specific example in Example 19 is not commensurate in scope with the broadly recited characteristics of the nucleic acid constructs of the instant claims and does not reasonably provide predictability of such a broad genus of nucleic acid constructs having the instantly desired function. Although applicant asserts that there is sufficient description for choosing intron sequences, there is not sufficient description for choosing intron sequences within the context of the instant invention, as it is not evident that insertion of any intron into any sequence encoding any intron, especially wherein the insertion is at any position, would result in the instantly recited outcomes. The instant claims are not closed to introns with any specific structural characteristic, as discussed above.

Applicant asserts that methods are well known in the art for introducing artificial introns. It is not disputed that methods are known in the art to introduce artificial introns. However, it is the unpredictable nature of introducing any intron into any nucleic acid sequence at any position that encodes any polymerase with a resultant incapability of the polymerase being expressed in any prokaryotic cell, whereas more than one copy of a nucleic acid sequence is produced when introduced into any eukaryotic cell. Furthermore, the claims recite that the gene product or protein expressed would be toxic specifically to a prokaryotic cell in the absence of the intron.

Applicant asserts that the claims are not directed to sequences encoding any polymerase; the polymerase must be incapable of being expressed in a prokaryotic cell and capable of producing more than one copy of a sequence when introduced to a eukaryotic cell. However, the instant specification does not describe a structural characteristic that sets forth which polymerases are and are not within this genus. Furthermore, claims 255, 262, and 265 are not even closed to sequences encoding a polymerase but rather any gene product.

Applicants' specifically claim that the inserted and inactivating intronic sequences will be spliced out, a process the specification indicates will be carried out by the cellular machinery that normally operates to splice introns out of pre-mRNA sequences. Applicants indicate that such splicing restores native activity to previously inactive proteins. However, the specification as filed does not provide any nucleic acid constructs for which this has actually been shown to demonstrate the predictability of such a broad mechanism. Applicant's specification does not provide sufficient

guidance or examples that would enable a skilled artisan to make the disclosed nucleic acid constructs containing sequences that are spliced out by cellular machinery without undue experimentation. Although the specification prophetically considers and discloses making and using such constructs, such a disclosure would not be considered enabling since introducing intervening sequences into nucleic acids alters their secondary structure, which makes their ability to be cleaved by the splicing machinery unpredictable. The specification has not resolved such issues, since no exemplified constructs that contain intervening sequences and are inactive therefore, and by which later processing inside the cell restores activity. Applicants have simply not shown that such intervening sequences can be spliced out to restore any activity to previously inactive polymerases (or any toxic protein for that matter).

Applicant points to Schwartz, Mayeda and Oshima for teachings of instances where introns have been inserted and spliced in eukaryotic cells and not in prokaryotic cells. It is acknowledged that insertion of an intron into a coding sequence may result in splicing of the sequence in eukaryotic cells. However, applicant is not enabled for inserting any intron into a sequence encoding any polymerase or any gene product with a predictable effect of capability of producing more than one copy of a sequence in a eukaryotic cell while being incapable of being expressed in a prokaryotic cell. The results of Mayeda and Oshima are not enabling for a method of inserting any intron into any polymerase or gene product with the instantly recited outcomes. Mayeda and Oshima teach that determinants essential for splicing are localized in the intron itself plus 3 nt of the 5' exon rather than the overall structure of the pre-mRNA. This does

not mean that the structure of the pre-mRNA is not important to the slicing process, just that the 3 nt of the 5' exon were more essential. Furthermore, Mayeda and Oshima are considered evidence that determinants/structure of the intron itself is crucial to the process, this supporting that not necessarily any intron would result in the instant outcomes when inserted into a nucleic acid encoding any gene product or polymerase. Furthermore, the 3 nt of the 5' exon were crucial for splicing, wherein instant claim 245, for example, embraces insertion anywhere in any sequence encoding any polymerase with the instantly recited outcomes. Although applicant argues that intron sequences inserted into a target gene at (C/A) AGG sites are likely to be spliced out, instant claim 245, for example, does not require this. Furthermore, Balvay et al. is evidence that the target structure does in fact play a role in splicing, as discussed above.

Applicant points to a statement of Balvay et al. "It is important to stress that in the absence of *in vivo* experiments or *in vitro* systems where transcription and splicing are coupled, all these conclusions about the functional significance of secondary structure should be taken as tentative ones." Although applicant interprets this statement as a tentative conclusion that is contrary to practical exercises that have been carried out generating *in vivo* data that introduction of introns into selected sites is a predictable art with a high likelihood of success, the statement of Balvay et al. actually supports the examiner's position. It is agreed that the issues of unpredictability due to secondary structure as taught by Balvay et al. could be overcome by *in vivo* experimentation, Balvay et al. is evidence that there are additional considerations such as secondary

structure that would lead to unpredictability, absence evidence to the contrary. The instantly recited constructs have extremely broad structural characteristics that were not enabled by the instant specification or the state of the art at the time of filing. Although applicant asserts that Balvay is directed to special occasions, a conclusion of lack of enablement means that, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation (see MPEP 2164.01(a)).

It is noted that introns can be inserted into genes to control the expression of the gene, as evidenced by the state of the art; (including Gatermann; and Yoshimatsu and Nagawa et al., as cited by applicant). However, none of the references are enabling for a broad method of inserting any intron into any position of any sequence encoding any gene product wherein the resultant eukaryotic sequence would express more than one copy of a sequence.

Again, the issue is not whether it was known in the art how to insert introns, but rather how to insert introns in a predictable fashion in accordance with the breadth of the instant claims and have the desired outcome specific to eukaryotic and prokaryotic cells with regards to any polymerase, as recited in the instant claims. Balvay et al. is simply an example that secondary structure is one complexity when considering splicing mechanisms.

In particular, it is demonstrated that the complex secondary structures of nucleic acids are responsible for their intron excision activity, and furthermore, that predicting the ability of the cellular splicing machinery to splice out precise intervening sequences

from disrupted sequences with variable secondary structures such that native activity is restored is considered unpredictable, because the splicing machinery is sensitive to the presence or absence of such structures.

Applicant relies on Lewin for teachings regarding experiments of splicing out a hybrid intron and teachings that splicing sites are generic, meaning that they do not have specificity for individual RNA precursors and the RNA precursors do not convey specific information (such as secondary structure) that is needed for splicing. The teachings of Lewin et al. do not diminish the unpredictability of the intron splicing mechanism when a non-native intron is inserted into a sequence having secondary structure. Simply because splice sites are generic to different sequences that do not "convey" secondary structure that is needed for splicing does not mean that the mechanism does not encounter problems of unpredictability as taught by Balvay et al.

Furthermore, the replacement of even a few nucleotides on an mRNA can abolish all activity of the translated protein. It is maintained that neither the specification nor the prior art arms one of skill with the information necessary to engineer sequences into nucleic acid constructs that will be reliably spliced out to result in a protein with native activity restored.

In order to practice the invention using the specification and the state of the prior art as outlined above, the quantity of experimentation required to practice the invention as claimed would therefore require the *de novo* determination of intervening sequences that can be fully spliced out without leaving behind any nucleotides that might interfere with native activity. In the absence of sufficient guidance from the specification, the

amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

MPEP 2164.01
Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, **when filed**, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention.

Also, MPEP 2164.01(a)
A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, **at the time the application was filed**, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 245, 247-255, 262 and 265 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1

and 2 of copending Application No. 11/929,055. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application '055 are directed to a construct comprising a nucleic acid encoding a polymerase and a non-native intron sequence wherein the polymerase is incapable of being expressed in a prokaryotic cell and is capable of producing more than one copy of a nucleic acid in a eukaryotic cell, which are each elements of the instant claims. Furthermore, each of the additional elements of the instant claims are embodiments of the '055 claims, as supported by the specification of application '055.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMY BOWMAN whose telephone number is (571)272-0755. The examiner can normally be reached on Monday-Thursday 6:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/AMY BOWMAN/

Examiner, Art Unit 1635